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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/783,571	02/20/2004	Paul B. Fisher	A34466-A-PCT-USA-A	2603

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/783,571	FISHER, PAUL B.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *1-44 and 46-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 7/24/2006.

Claims 1-50 are currently pending and are addressed herein.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 5/27/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Election/Restrictions

Applicant's election of Group III (claim 45) in the reply filed on 7/24/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-44 and 46-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 7/24/2006.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 45 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompass nucleic acid encoding MDA-7 protein. The specification indicates:

> "The term 'MDA-7' as used herein refers to a protein having essentially the amino acid sequence set forth as SEQ ID NO: 2, having Genbank Accession Number U16261. A nucleic acid encoding MDA-7 may have the coding sequence as set forth in SEQ ID NO: 1, Genbank Accession No. U16261, or another sequence which, when translated, produces a protein having essentially the same amino acid sequence. It should be noted that the portion of the nucleic acid sequence presented as SEQ ID NO: 1 which constitutes the protein encoding region extends from nucleotide 275 to nucleotide 895. The scope of the invention embraces functional equivalents of the nucleic acid and protein which vary in insignificant ways from the native molecules; for example, it includes isolated nucleic acids which hybridize to the nucleic acid sequence set forth as SEQ ID NO: 1 under stringent hybridization conditions..." (Emphasis added; see page 18, lines 4-15 of the specification).

Therefore, the claims encompass a genus of nucleic acid molecules which encode variants of"MDA-7 protein" wherein the "MDA-7 protein" can be different from the polypeptide disclosed as SEQ ID NO: 2. Considering that the specification clearly indicates that the invention embraces functional equivalents of the nucleic acid and protein including isolated nucleic acids

which hybridize to the nucleic acid sequence set forth as SEQ ID NO: 1 under stringent hybridization conditions, the claims encompass a genus of molecules which includes an enormous number of different species molecules.

It is noted that the claims do not require that the nucleic acids possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of molecules that is defined merely by their ability to hybridize to the nucleic acid sequence set forth as SEQ ID NO: 1 under stringent hybridization conditions. There is no indication in specification or prior art which indicates that any nucleic acid sequence other than a nucleic acid sequence encoding SEQ ID NO: 2 has been delivered to a cancer cell having a mutant ras gene, or to a pancreatic cancer cell or that any such variant could be used to inhibit proliferation or treat said cancer cells.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only distinguishing characteristic of the genus of molecules encompassed by the claims disclosed in the specification is that the nucleic acid hybridizes to SEQ ID NO: 1 under stringent hybridization conditions.

The specification does not identify any particular portion or critical elements of the nucleic acid molecule or the encoded MDA-7 protein that must be conserved. Therefore, the claims encompass nucleic acid molecules which encode proteins that may have different

functions than the MDA-7 polypeptide disclosed as SEQ ID NO: 2, or which may be non-functional variants.

Accordingly, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

Therefore, only isolated nucleic acids encoding the amino acid sequence set forth in SEQ ID NO: 2 meet the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 45 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-14 and 16 of U.S. Patent No. 5,710,137 in view of Saison-Behmoaras et al. (EMBO J., 1991; 10(5):1111-1118) and further in view of WO 97/16547 A1 (Roth et al.).

The instant claims are drawn to a viral vector comprising a nucleic acid sequence encoding *MDA-7* protein and a nucleic acid encoding an antisense *ras* nucleic acid molecule, each operatively linked to a promoter element.

An obvious-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patently distinct from the reference claims(s) because the examined claims are either anticipated by, or would have been obvious over, the reference claim(s). See e.g., *In re Berg,* 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman,* 11 F.3d1046, 29 USPQ2d 2010 (Fed. Cir.) 1993).

Here claims 12-14 and16 of U.S. Patent No. 5,710,137 are drawn to a composition comprising a nucleic acid comprising an MDA-7 gene, wherein the nucleic acid is comprised in a vector, wherein the vector is a viral vector such as an adenoviral vector.

The indicated claims of U.S. Patent No. 5,710,137 differ from the instant claims of the examined application in that the claims of U.S. Patent No. 5,710,137 fail to disclose that the viral vector further comprises an antisense *ras* nucleic acid molecule.

Saison-Behmoaras et al. teaches that an antisense-*ras* oligonucleotide which hybridizes to a *RAS* nucleic acid molecule and inhibits translation of *ras*-specific mRNA (specifically and antisense-Ha-*ras* oligonucleotide that inhibits translation of Ha-*ras* mRNA) can be used to inhibit the proliferation of cells having a mutant Ha-*ras* gene (i.e., an oncogenic Ha-ras gene) (e.g., see p. 1111, abstract; p. 1116, first column of text and Figure 6; etc.).

Saison-Behmoaras et al. does not teach that the antisense oligonucleotide can be delivered using an adenoviral vector.

WO 97/16547 A1 (Roth et al.) teaches the use of an adenoviral vector to deliver and express an antisense oligonucleotide in a cancer cell. Specifically, Roth teaches an adenoviral vector that expresses an antisense-K-ras oligonucleotide wherein the vector can be used to deliver and express the antisense oligonucleotide in a cancer cell (e.g., see abstract; page 4, lines

6-16; the paragraph bridging pages 4-5; Examples 3 and 4, pages 53-55; etc.). Furthermore, Roth explicitly teaches antisense therapy in combination with other gene therapies and indicates that the combination therapy may produce an improved anticancer treatment (see page 44 lines 14-24). Roth also teaches that the expression vector will be an efficient method for delivering a therapeutically effective gene to counteract clinical disease (see page 43, lines 25-29).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to modify the indicated claims of U.S. Patent No. 5,710,137 such that the adenoviral viral vector which comprises the MDA-7 gene further comprises and expresses an antisense-*ras* oligonucleotide such that the adenoviral vector encodes and expresses both the antisense-ras oligonucleotide and the MDA-7 protein with a reasonable expectation of success.

One of skill in the art would have been motivated to combine the references to create claimed invention because: (1) Roth teaches an adenoviral vector that encodes and expresses an antisense oligonucleotides can be used in combination with other therapies including gene therapy, (2) Roth specifically teaches that the viral vector encoding the antisense nucleic acid can further comprise and express other genes of interest (e.g., see page 33, lines 28-31; page 34, lines 2-4; page 39, lines 5-11; and page 44, lines 14-24), (3) the claims of U.S. Patent No. 5,710,137 teach an adenovirus vector which encodes and expresses the MDA-7 gene can be used as a anticancer agent, and (4) Saison-Behmoaras teaches that *ras* antisense oligonucleotides can be used as anticancer agents (e.g., see Figure 1 of U.S. Patent 5,710,137 as well as Figure 6 of Saison-Behmoaras).

MPEP 2144.06, in discussing art-recognized equivalence for the same purpose, mentions *In re Kerkhoven*, wherein the court expressed the following:

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose...[T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven* 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

In the instant case, the claims of U.S. Patent 5,710,137 and the antisense *ras* oligonucleotides of Saison-Behmoaras are considered to be two compositions each of which is taught by the prior art to be useful for the same purpose (treating cancer).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 45 is rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent No. 5,710,137 in view of Saison-Behmoaras et al. (EMBO J., 1991; 10(5):1111-1118) and further in view of WO 97/16547 A1 (Roth et al.).

The applied reference (U.S. Patent No. 5,710,137) has a common inventor with the instant application. Based upon the publication date of the patent, it constitutes prior art under 35 U.S.C. 102(b). Therefore, this rejection under 35 U.S.C. 103(a) is not subject to exclusion/disqualification under 35 USC 103(c) See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The instant claims are drawn to a viral vector comprising a nucleic acid sequence encoding *MDA-7* protein and a nucleic acid encoding an antisense *ras* nucleic acid molecule, each operatively linked to a promoter element.

U.S. Patent No. 5,710,137 teaches a composition comprising a nucleic acid comprising an MDA-7 gene, wherein the nucleic acid is comprised in a vector, wherein the vector is a viral vector such as an adenoviral vector (e.g., see claims 12-14 and 16).

U.S. Patent No. 5,710,137 fails to disclose that the viral vector further comprises an antisense *ras* nucleic acid molecule.

Saison-Behmoaras et al. teaches that an antisense-*ras* oligonucleotide which hybridizes to a *RAS* nucleic acid molecule and inhibits translation of *ras*-specific mRNA (specifically and antisense-Ha-*ras* oligonucleotide that inhibits translation of Ha-*ras* mRNA) can be used to inhibit the proliferation of cells having a mutant Ha-*ras* gene (i.e., an oncogenic Ha-ras gene) (e.g., see p. 1111, abstract; p. 1116, first column of text and Figure 6; etc.).

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14-24). Roth also teaches that the expression vector will be an efficient method for delivering a therapeutically effective gene to counteract clinical disease (see page 43, lines 25-29).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to combine the teachings of U.S. Patent No. 5,710,137, Saison-Behmoaras et al. and WO 97/16547 A1 (Roth et al.), to make an adenoviral viral vector which comprises and expresses (1) the MDA-7 gene, and (2) an antisense-*ras* oligonucleotide with a reasonable expectation of success.

One of skill in the art would have been motivated to combine the references to create claimed invention because: (1) Roth teaches an adenoviral vector that encodes and expresses an antisense oligonucleotides can be used in combination with other therapies including gene therapy, (2) Roth specifically teaches that the viral vector encoding the antisense nucleic acid can further comprise and express other genes of interest (e.g., see page 33, lines 28-31; page 34, lines 2-4; page 39, lines 5-11; and page 44, lines 14-24), (3) the claims of U.S. Patent No. 5,710,137 teach an adenovirus vector which encodes and expresses the MDA-7 gene can be used as a anticancer agent, and (4) Saison-Behmoaras teaches that *ras* antisense oligonucleotides can be used as anticancer agents (e.g., see Figure 1 of U.S. Patent 5,710,137 as well as Figure 6 of Saison-Behmoaras).

MPEP 2144.06, in discussing art-recognized equivalence for the same purpose, mentions *In re Kerkhoven*, wherein the court expressed the following:

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the

very same purpose...[T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven* 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

In the instant case, the claims of U.S. Patent 5,710,137 and the antisense *ras* oligonucleotides of Saison-Behmoaras are considered to be two compositions each of which is taught by the prior art to be useful for the same purpose (treating cancer).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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PATENT EXAMINER